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Role of Sirtuin 1 in the phenotype and functions of dendritic cells in the context of transplantation of obese animals

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Biography

Jean de Lima holds the title of Biotechnologist from the Pontifical Catholic University of Paraná (PUC-PR), where he worked with in vitro analysis of Campomanesia xanthocarpa extract in cell activation in HUVECs and THP-1 strains and is a collaborator to investigate biogenesis of circular RNA in humans. Currently, he is conducting an internship program at Lausanne University in Switzerland and is also active in humanitarian activities teaching guitar and informatics to special students.

Abstract

Sirtuin 1 (SIRT1) is a class 3 Histone Deacetylase (HDAC3) that acts primarily by regulating T cell differentiation, proliferation and activation, therefore disable transcriptions of genes in Dendritic Cells (DCs) that are important for T cell activation and differentiation of effector cells in graft rejection and in other chronic inflammatory processes like obesity. Therefore, our hypothesis that the obesity influences the differential expression of sirtuin 1 (SIRT1) in DCs, changing its phenotype and function, and thus T cell activation, exacerbating the allograft immune response. Thus, our goal was to specifically investigate the role of SIRT1 in the function, phenotype and the implications on DCs metabolism, and if it can affect T cell functions in the context of skin transplantation in obese animals. We saw the impact of absence of SIRT1 in the mitochondrial metabolism of DCs (by Seahorse technology) in animals with specific deletion of SIRT1 gene in DCs (CD11cCreSIRT1fl ox/flox). In addition, we observed after treatment with a SIRT1 agonist (resveratrol, 50 nM) in Bone Marrow-Derived DC (BMDCs) incresead of protein expression of TGF-β, IDO and the decreased of costimulatory molecules (CD40, CD80, CD86) with parallel induction of SIRT1. In a hyperlipid diet-induced obesity (HFD) mode plus tranplantation, we observed that DCs from obese animals and with skin graft had the most lower SIRT1 expression and this led to a more pro-inflammatory profile as well as less glycolytic metabolic profile and relation with tryptophan metabolism, which is characteristic of a DC tolerance according to the literature. Based on the results obtained so far, we can suggest that increased expression of SIRT1 by resveratrol treatment leads to a more tolerogenic profile in BMDCs and DC, which may influence CD4+ T cell proliferation and polarization and consequently an improvement in the graft acceptance in obesity.

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